A component of the mir-17-92 polycistronic oncomir promotes oncogene-dependent apoptosis.

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Public Summary:
mir-17-92, a potent polycistronic oncomir, encodes six mature miRNAs with complex modes of interactions. In the Emu-myc Burkitt's lymphoma model, mir-17-92 exhibits potent oncogenic activity by repressing c-Myc-induced apoptosis, primarily through its miR-19 components. Surprisingly, mir-17-92 also encodes the miR-92 component that negatively regulates its oncogenic cooperation with c-Myc. This miR-92 effect is, at least in part, mediated by its direct repression of Fbw7, which promotes the proteosomal degradation of c-Myc. Thus, overexpressing miR-92 leads to aberrant c-Myc increase, imposing a strong coupling between excessive proliferation and p53-dependent apoptosis. Interestingly, miR-92 antagonizes the oncogenic miR-19 miRNAs; and such functional interaction coordinates proliferation and apoptosis during c-Myc-induced oncogenesis. This miR-19:miR-92 antagonism is disrupted in B-lymphoma cells that favor a greater increase of miR-19 over miR-92. Altogether, we suggest a new paradigm whereby the unique gene structure of a polycistronic oncomir confers an intricate balance between oncogene and tumor suppressor crosstalk.

Scientific Abstract:
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